REMARKS

Upon entry of the present amendment, claims 24-75 will be pending. Claims 1-10, 13, 15, 16, 18-23, and 76 have been canceled without prejudice or disclaimer. Applicants hereby reserve the right to pursue the canceled subject matter in a continuing application.

I. Summary of Interview

Applicants would like to thank Examiners Spiegler, Hutzell, and Benzion for the interview accorded on June 26, 2002, a summary of which was attached to Paper No. 10. To the extent that it may be required, Applicants provide a brief summary of this interview below.

During the interview, Examiners Spiegler, Hutzell, and Benzion indicated that the use of SEQ ID NO: 56 as a marker for B cell lymphoma was sufficient to overcome the rejection of all the pending claims under 35 U.S.C. § 101.

II. Rejection of the Claims Under 35 U.S.C. § 101

Claims 24-75 were rejected under 35 U.S.C. § 101 for allegedly lacking patentable utility. *See* Paper No. 11, page 3, first paragraph. More specifically, while the Examiner admits that the asserted utility as a B cell lymphoma marker is specific (see page 3, paragraph 6 of Paper No. 11), the Examiner states "[t]he specification does not assert a substantial utility because the utilities asserted by Applicants requires or constitutes carrying out further research to identify or reasonably confirm a 'real world' use." *See* Paper No. 11, page 3, fifth paragraph.

Applicants respectfully disagree and traverse.

Applicants note that the Utility Guidelines instruct that for substantial utility, "an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a real world context of use..." (see page 2100-32 of M.P.E.P. §2107.1 (I)). The M.P.E.P. further instructs that "... any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a 'substantial' utility."

Applicants have set forth in the specification statements that clearly provide the substantial utility that the Examiner contends is lacking. Specifically, the specification discloses that the gene is expressed primarily in B-cell lymphoma, therefore the claimed polynucleotides and polypeptides could be useful as reagents for differential identification

and diagnosis of immune disorders and cancers (*see*, specification, page 36, lines 6-9), especially in the diagnosis and/or treatment of B cell lymphomas. Therefore, Applicants have disclosed the correlation of the claimed invention to a particular disease condition (e.g., being primarily expressed in B cell lymphoma), thereby fully satisfying the substantial prong of the utility requirement.

Furthermore, case law has held that pharmacological or therapeutic inventions that provide any "immediate benefit to the public" satisfy 35 U.S.C. § 101. *See*, *Nelson v. Bowler*, 626 F.2d 853, 856, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980); *See also,* M.P.E.P. §2107.01(III). It is well-established that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and satisfies the utility requirement. *Id.* With respect to the relevance of the asserted use to the identification of an activity, all that is required of Applicants is that there be a reasonable correlation between the biological activity and the asserted utility. *See*, *Nelson v. Bowler*, 626 F.2d 853, 857 (C.C.P.A. 1980). Such a correlation is given by the unique tissue distribution of the claimed polypeptides of the invention. Accordingly, the utilities asserted by Applicants are clearly substantial.

Furthermore, the Examiner asserted that Applicants did not show any evidence that the gene is "differentially" expressed in the B cell lymphomas (*see*, Paper No. 11, page 5, first full sentence). Applicants respectfully disagree and traverse. On page 36, lines 6-9 of the specification, it is asserted that the gene is primarily expressed in B cell lymphoma. Applicants respectfully submit that one of skill in the art would clearly recognize that such a statement conveys that differential expression exists for the claimed invention, as required by the Utility Guidelines (see page 2100-38, M.P.E.P. §2107.02(A)). Nevertheless Applicants have submitted herewith an executed declaration under 37 C.F.R. § 1.132 of Dr. George Komatsoulis, from Human Genome Sciences, Inc. The executed declaration under 37 C.F.R. § 1.132 indicates that the expression of the polynucleotide of SEQ ID NO: 56 was assessed in B cell lymphoma, as well as many other normal, non-leukemic B cells and hematopoetic cells (*e.g.,* T cells, B cells, monocytes). Based on this assessment, the expression was preferentially observed in B cell lymphoma. Thus, given this preferential expression in B cell lymphoma cells *versus* normal B cells, one of skill in the art would readily believe that the polypeptide encoded by SEQ ID NO: 56 could be used as a diagnostic marker for B cell lymphoma as asserted in the specification and as attested in Dr. Komatsoulis' executed declaration.

Applicants note that the Examiner asserted that "evidence of a differential expression might serve as a basis for use of the claimed polypeptide as a diagnostic for a disease" (see page 5 of Paper No. 11, first paragraph). In view of the above, Applicants submit that such evidence was originally disclosed in the specification further corroborated by Dr. Komatsoulis's Rule 132 declaration. Therefore, the utility requirement under 35 U.S.C. §101 is satisfied.

The Office Action further states that "no protein expression data of SEQ ID NO: 56 is provided. That is, the specification is silent as to any expression patterns of SEQ ID NO: 56." *See* Paper 11, page 4, first paragraph. Applicants disagree and traverse. Applicants provide herewith Exhibit A, taken from the sequence listing of SEQ ID NO: 56, which shows that the gene of the invention includes all the elements recognized by one skilled in the art to be necessary for its translation, *i.e., e.g.*, an octamer transcription element (located approximately 130 base pairs upstream from the initiation codon), which is the binding site of the transcription factor Oct-1, a TATA box signal (located approximately 11 base pairs upstream from the initiation codon), which is responsible for the correct positioning of transcription factors and RNA polymerase, an initiation codon (ATG), a stop codon (TAG), and a polyA signal (AAUAAA, located approximately 540 base pairs downstream from the stop codon). Therefore, it would be evident to one skilled in the art that the gene of the invention would be more likely than not translated into protein. The presence of these elements, in addition to the teaching that this gene is primarily expressed in B-cell lymphoma, supports Applicants' assertion that the claimed protein is likely expressed in the disease state and could therefore be used as a marker for B cell lymphoma.

In support of these observed characteristics, Applicants hereby submit a Rule 132 declaration executed by Dr. G. Komatsoulis, who attests that he observed all these features in the disclosed cDNA and therefore believe that the polynucleotide would be properly translated (*see*, paragraph 5 of the attached declaration). Therefore, simply by examining the sequence of the gene of the invention, originally filed with the application, one of skill in the art would clearly understand that a polypeptide would be translated from the disclosed gene.

The Examiner equates the present situation to the one described in *Brenner v. Manson* (383 U.S. 519 (U.S. 1966)). *See*, Paper 11, page 5, first paragraph, last sentence. Contrary to the Examiner's allegation, the instant case is not analogous to the situation in *Brenner*, where the issue was not whether a disclosed utility was sufficient. Rather, the

applicant was trying to establish an earlier date of invention for the purpose of provoking an interference (*Id.* at 521). Indeed, in *Brenner* the Examiner's initial basis for refusing to declare an interference was that the applicant had failed to disclose any utility at all (*Id.* at 521). Thus, the issue in *Brenner* was whether the applicant had made an adequate "showing" to establish a prior date of invention, *i.e.*, whether "the process claim has been reduced to production of a product shown to be useful" through actual demonstration of the utility (*Id.* at 534). The only evidence offered by the applicant to make this showing was a reference to an article by a third party showing the activity of an adjacent homologue of the subject steroid compound (*Id.* at 521-522). The appellate court agreed that the applicant had done nothing to show or demonstrate that the compound was indeed useful (*Id.* at 521). Thus, it upheld the rejection of the request for declaration of an interference (*Id.* at 536).

In contrast, the issue in the present case is whether the instant application explicitly teaches at least one utility that meets the requirements of § 101. For the reasons stated above and below, Applicants respectfully submit that such a utility exists.

The Office Action further contends that the claimed utilities do not correspond to well-established utilities because "one of ordinary skill in the art would not immediately appreciate why the invention is useful based on the characteristics of the invention." *See*, Paper 11, page 6, item II. Applicants respectfully disagree and traverse. For the reasons articulated above and based upon Dr. Komatsoulis's Rule 132 declaration, Applicants respectfully submit that the claimed invention has a well-established utility. The Revised Interim Utility Guidelines Training Materials defines a well-established utility as a utility which "does not encompass any 'throw away' utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA." The Examiner has recognized that "Applicants' assertion that SEQ ID NO: 56 may be used as a marker for B-cell lymphoma can be considered as a specific utility." *See*, Paper No. 11, page 3, fourth paragraph. Therefore, the use of the claimed polypeptides as markers for B-cell lymphoma would not be considered by one of skill in the art as a "throw away" utility because of the clear implications in diagnosing and/or treating the disease in affected individuals based on the disclosure.

Applicants submit that, for the reasons stated above, the utility asserted in the specification for SEQ ID NO: 56 is indeed *substantial and/or well-established.* Accordingly, Applicants respectfully submit that the rejection of claims 24-75 under 35

U.S.C. § 101 has been obviated. Applicants respectfully request that the rejection of claims 24-75 under 35 U.S.C. § 101 be reconsidered and withdrawn.

III. Claims Rejection under 35 U.S.C. § 112, first paragraph

Claims 24-75 are also rejected under 35 U.S.C. § 112, first paragraph. *See*, Paper 11, page 7, item 7. Specifically, the Office Action asserts "since the claimed invention is not supported by a substantial or well-established utility for the reason set forth above, one skilled in the art clearly would not know how to use the claimed invention." *See,* Paper No. 11, page 7, item 7.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific, substantial and credible asserted utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. §101 rejection is proper." M.P.E.P. § 2107 (IV) at 2100-36. Therefore, because the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejections under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be withdrawn. Accordingly, Applicants respectfully request that the rejection of claims 24-75 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

CONCLUSION

Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application. Applicants believe that this application is in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Dated: August 27, 2003

Respectfully submitted,

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Docket No.: PZ040P1

Ruben, et al.

Application No.: 09/726,643 Group Art Unit: 1637

Filed: December 1, 2000 Examiner: A. Spiegler

For: **26 Human Secreted Proteins**

Commissioner for Patents
Washington, D.C. 20231

Declaration of Dr. George Komatsoulis Under 37 C.F.R. § 1.132

I, George Komatsoulis, do hereby declare and say:

1. I am a citizen of the United States, residing at 9518 Garwood Street, Silver Spring, MD, 20901.

2. I obtained a Ph.D. in Molecular Biology and Biochemistry from the California Institute in Technology in 1993. I have 19 years of experience in the field of molecular biology.

3. Since February 3, 1997, I have served as a scientist of Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, Maryland 20850, assignee of the captioned application.

4. I have personal knowledge that the expression of the polynucleotide of SEQ ID NO: 56 was assessed in several hundreds of libraries representing immune and non-immune human tissues, and based on this assessment, expression of the polynucleotide of SEQ ID NO: 56 was only observed in B cell lymphoma cells. More specifically, the expression was

preferentially observed in B cell lymphoma cells, as opposed to normal non-leukemic B cells and hematopoetic cells.

5. I have reviewed the nucleotide sequence of the polynucleotide of SEQ ID NO: 56 and, based on the following characteristics, I believe that this polynucleotide will be properly translated into a polypeptide:

(a) the polynucleotide possesses an initiation (ATG) and a termination (TAG) signal, defining a long Open Reading Frame from nucleotide 265 to nucleotide 504 of SEQ ID NO: 56, as shown in attached **Exhibit A**;

(b) the polynucleotide exhibits a long coding region, which encodes a polypeptide of 79 amino acids, as shown in attached **Exhibit A**; this indicates that the polynucleotide is unlikely to be non-coding;

(c) the polynucleotide possesses an Oct-1 transcription factor recognition sequence located from nucleotide 130 to 138 of SEQ ID NO. 56 (135 bases upstream from the initiation codon);

(d) the polynucleotide possesses a TATA box signal at nucleotide 151-155 (14 bases upstream from the initiation codon);

(e) the polynucleotide possesses a polyadenylation signal (AATAAA) at position 1046-1051 of SEQ ID NO: 18, as shown in attached **Exhibit A**; and

(f) the polynucleotide does not possess repeated AUUUA motifs in its un-translated 3' end, which would indicate that the corresponding mRNA is unstable.

Therefore, in view of the observed characteristics of the polynucleotide of SEQ ID NO: 56, I believe that the polynucleotide of the invention will be translated into a polypeptide.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so

made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States code and that such willful false statements may jeopardize the validity of the application of any patents issued thereupon.

Dr. George Komatsoulis

26 Aug 03
Date

Exhibit A

ccacgcgtcc gcaaccaggt tcaagacgag taagaggaat gcaagttatc tttttccaaa 60

aagaattgtt ttcaatttaa ttaagtttta aattcgaaag gagaataatg gctcatgtaa 120

aatgtgggc atttgcaaata agtaatatga ttgtgtgtgt gtctgtgggc atgtgtgtat 180

gacagagaga gagggagaga gagacagaga gagagagtca gtggtcagtg tctgtggatt 240

tggggacagg atatattatg atac **ATG** gtc ccc tgg ttc ctt ctt tgg agt tcc ttc ttc 300
M V P W F L L W S S F F

ata ggc aca tca tca gcc tat att gac aaa cag gta aag att gtt aga caa aaa tct 357
I G T S S A Y I D K Q V K I V R Q K S

acc tat tgg gga gaa aaa ttt tta aaa aga tgt gaa agg gaa aga ata aaa gag agt 414
T Y W G E K F L K R C E R E R I K E S

gaa caa tca ggc aag aga gga gaa tta aga gaa aga cag caa aag tca aat gaa gca 471
E Q S G K R G E L R E R Q Q K S N E A

ggc tgc atc tat cag tcc att ata ctc att **TAG** gggtgt aagtgtgctt ctctgaatct 530
G C I Y Q S I I L I *

gagagagtca gagtctttta agaaaggaag aattcaagat tttgcaatat ctattaggta taagaatgta 600

ttttttaaaa gttaagcaat tccaggcaac aacacatatc agatgcatgt tgtgggcaga 660

gccagggtag caagcttagg gaatcactgc aaagaaaatt gtatgtggac tttgggtttg 720

tacttgaggc aggtagacaa atatgtatga aactgtgttt gacataccta acaaaaatcc 780

atcaatggga atttctccta ccacagcatt gcttcattgc tgacataaat gggacagaaa 840

ggaaatcttt ttttaaaaaa aaattaataa ctagttaagg ctaggatgga ataatgtgtg 900

gtgctctgcc ttgttccctg atgacatttc cattttttcta aggaagaaat ctctattgat 960

ttagttttgc ctgattataa aagtaataca aatttctttc tcaaaatgca tacaaca 1017

aataaaaattgat gaaaatcaaa aaaaaaaaaa aa 1052

Sequence analysis of SEQ ID NO: 21 (encoding SEQ ID NO: 56).

The recognition sequence for the transcription factor Oct-1 is shown boxed/shaded, the TATA Box is boxed, and the putative polyadenylation signal is shown **bold**.